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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|----------------------|------------------|
| 09/987,455 | 11/14/2001 | Jiradej Manosroi | 0652.2190001/EKS/Y-W | 6739 |
| 26111 | 7590 | 05/04/2004 | EXAMINER | |
| STERNE, KESSLER, GOLDSTEIN & FOX PLLC 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005 | | | NASHED, NASHAAT T | |
| | | | ART UNIT | PAPER NUMBER |

1652

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--|--|--|
| Office Action Summary | Application No. 09/987,455 | Applicant(s) MANOSROI ET AL. | |
| | Examiner Nashaat T. Nashed, Ph. D. | Art Unit 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 40-60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 40-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>2/4/04</u> . | 6) <input type="checkbox"/> Other: _____ |

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The application has been amended as requested in the communication filed February 4, 2004. Accordingly, claims 1-39 have been canceled, and claims 40-60 have been entered.

Claims 40-60 are pending and under consideration in this Office action.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. 112, first paragraph, as the specification lacks a sufficient written description for enablement based on deposit requirement for the reasons set forth in the prior Office action mailed September 12, 2003.

Claim 57 is rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

Applicants argue that disclosure the specification contains adequate written description and the vector pComb3H-K2S. Applicants argue that they merely inserted the coding sequence for K2S in the pComb3HSS phagemid, which had been provided by Dr. Carlos F. Barbas.

Applicants' arguments filed 2/4/04 have been fully considered but they are not deemed to be persuasive. The pComb3HSS phagemid is not available to the public because the record contains no commitment from Dr. Barbas to provide the said phagemid to the public. Thus, the deposit requirement remains proper.

Claims 1-15, 17-24 and 31-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The phrases "a tPA variant" and "a K2S variant" in new claim 40 render the claim indefinite for the reasons set forth in the prior Office action mailed September 12, 2003.

Applicants argue that specification defines the variants.

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Applicants' arguments filed 2/2/95 have been fully considered but they are not deemed to be persuasive. While it is true that the specification attempted to define the terms, the definitions are indefinite by themselves because they contain open-ended language. They include phrase such as "the variants may include one, several or all", see page 11, paragraph 39, and "SEGN or a variant or fragment, a functional variant, an allelic variant, subunit, a chemical derivative, a fusion protein, or a glycosylation variant thereof", see page 16, paragraph 56.

- (f) The phrase "pComb3HSS" renders claim 57 indefinite for the reasons set forth in the prior Office action mailed September 12, 2003. The specification does not identify either the method of constructing pComb3HSS phagemid or its source, see the discussion above regarding applicants' response to the rejection under 35 U. S. C. 112, First paragraph.
- (k) Claim 51 is indefinite because the claim does not define wash conditions. The sentence bridging pages 14 and 15 states clearly that the degree of stringency is decided in the washing step. Thus, without the washing step the claim is considered indefinite.
- (l) Claims 41-43, 52-56 and 58-60 are included with this rejection because they are dependent on rejected claims and do not cure the deficiencies of the claim from which they are dependent.

New Rejection:

- (J) Claim 44 is confusing because, if the tPA variant of (b) is any of the finger domain, the Growth factor domain, the kringle domain 1 or 2, the resulting protein would not be expected to have thrombolytic activity for the lack of the protease domain.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed

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invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 40-56 and 58-60 are rejected under 35 U.S.C. 103 as being unpatentable over Wang *et al.* (IDS Document AM1: EP 0357391 A2) in view of Obukowicz *et al.* (IDS reference AR9: Biochemistry 1990, 29, 9737-9745), Niwa *et al.* [U. S. Patent 5,840,533 (533)] and the well known nucleic acid encoding human tissue plasminogen activator for the reasons set forth in the prior Office action mailed September 12, 2003.

Applicants argue that none of the cited references teach the claimed invention because the references, when combined, must teach all the claim limitation.

Applicants' arguments filed 2/4/04 have been fully considered but they are not deemed to be persuasive. The examiner agrees with applicant that none of the references teach the claimed invention as evidenced by the fact that the rejection were made under 35 U. S. C. 103. In rejecting the claims in the previous Office action, the examiner has set a clear *prima facie* case of obviousness showing that the prior art provide motivation to combine the individual references and teach all the elements of the claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The '533 patent provides one of ordinary skill in the art with motivation to obtain the variant taught in the patent in large quantity as it teaches longer half-life time of the variants and greater thrombolytic activity. Also, the '533 patent suggests the expression of the variants in *E. coli* fused to a signal peptide for translocation of the variant tPA. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to attach the coding sequence OmpA to the nucleic acid sequence of SEQ ID NO: 1 of the '533 patent by well known methods in the art (claim 40-51), inserted in well known vector under the control of the well known lac operator (52-56 and 60), transform a host *E. coli* cell (claims 58 and 59), and utilize the host cell in a method to make the variant tPA as taught by Wang *et al.* It should be noted that the nucleic acid constructed by the ordinary skilled in the art would contain the nucleic acid of SEQ ID

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NO: 1 and SEQ ID NO: 20 (claims 42 and 43), and has the nucleic acid sequence of SEQ ID NO: 3 (claim 41). All the K2S variant of SEQ ID NO's: 11-18 are well known in the prior art with known benefits as well as all the tPA fragments comprising the protease domain of SEQ ID NO: 19 in claims 44, and 47-50. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 40-60 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-18, 21-29, and 31-53 of copending Application No. 09/987,457 ('457). Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the '457 application are directed to making proteins in prokaryotic cells including the product of claims 40-60 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the


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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Nashaat T. Nashed, Ph. D.
Primary Examiner
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